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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,093	08/22/2000	Johnathan A. Napier	00487.00001	1868

22907 7590 06/10/2003

BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER

WALICKA, MALGORZATA A

ART UNIT PAPER NUMBER

1652

DATE MAILED: 06/10/2003

67

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/555,093

Applicant(s)

NAPIER, JOHNATHAN A.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 23 and 39-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 39-41 and 43 is/are allowed.
- 6) ☒ Claim(s) 1-12, 14, 23 and 42 is/are rejected.
- 7) ☒ Claim(s) 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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The Amendment and Response filed on Jan. 13, 2003 as paper No. 16 is acknowledged. The amendments have been entered as requested. Claims 15-22 and 24-38 are cancelled. Claims 1 and 13 are amended; claims 39-43 are added. Claims 1-14, 23 and 39-43 are pending and are the subject of this Office Action.

Detailed Office Action

1. Objections

Claim 8 is objected to, because the abbreviation GLA is not expanded. An abbreviation used in the claims for the first time should be expanded.

2. Rejections

2.1. 35 U.S.C. section 101

Rejection of claims 1-14 and 23 made in the previous Office Action paper No.14 is withdrawn, because claim 1 has been amended.

2.2. 35 U.S.C. section 112, second paragraph

Rejection of claim 1 made in the previous Office Action paper No. 14 is withdrawn, because the claim has been amended.

New rejection

Claim 14 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to the claimed desaturase of claim 1 wherein said desaturase is covalently linked to a moiety. The term "moiety" is indefinite rendering the claim indefinite. On page 6, line 24, Applicants write, "where a polypeptide is linked to a moiety capable of being isolated by affinity

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chromatography." This sentence is not a proper definition of the term "moiety" because it is unknown what is included or excluded from the scope of the term.

Claim 23, which provides for the use of desaturase, disclosed in medicine, is unclear how the polypeptide of claim 1 is further limited. Please note, that the statement of intended use is not a limitation on product. If Applicants intend a pharmaceutical composition, they should claim it as "A pharmaceutical composition comprising the polypeptide of claim 1."

2.3. 35 U.S.C. section 112, first paragraph

2.3.1. Lack of written description

The amended claims 1-12, 14 and 23 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons stated in the previous Office Action and reiterated herein.

The claims are directed to a polypeptide having desaturase activity, which comprise:

- b) has one or more amino acid deletions, insertions or substitutions relative to SEQ ID NO: 2, but has at least 50% amino acid sequence identity therewith;
- c) is a fragment of SEQ ID NO: 2 or polypeptide b) which is at least 150 amino acids long.

Claims 1-12, 14 and 23 are directed to any polypeptide comprising variants of SEQ ID NO: 2 that are at least 50% identical to SEQ ID NO: 2 and to any polypeptide comprising at least 150 amino acids long fragments of SEQ ID NO: 2, or a 150 amino acid long fragment of a sequence that is at least 50% identical to SEQ ID NO: 2, or to a fragment of SEQ ID NO: 2, wherein said polypeptide has desaturase activity. Claims 1-12, 14 and 23 are rejected under this section of 35 USC 112, because the claims are

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directed to a genus of polypeptides derived from SEQ ID NO: 2 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO: 2 and fragments of SEQ ID NO: 2 that have not been disclosed in the specification or fragments that are derived from variants of SEQ ID NO: 2 having at least 50% identity to SEQ ID NO: 2. No description has been provided of the modified polypeptide sequences encompassed by the claim.

The amino acid sequences comprising an amino acid sequence that is at least 50% identical to SEQ ID NO: 2 or comprises at least 150 amino acid fragment of SEQ ID NO: 2, or comprises at least 150 amino acid fragment of a sequence that is in 50% identical to SEQ ID NO: 2, belong to a large and variable genus of polypeptides. A sufficient written description of the genus can be achieved by a recitation of a representative number of polypeptides defined by amino acid sequence or a recitation of structural features common to members of the genus, **which features constitute a substantial portion of the genus**. The recited structural feature of the genus, i.e., a fragment of SEQ ID NO: 2 being at least 150 amino acid long, or a sequence being at least 50% identical to SEQ ID NO: 2, or its fragment that is at least 150 amino acid long, do not constitute a substantial portion of the genus. In addition, Applicants fail to describe the at least 150 amino acid fragment of SEQ ID NO: 2 that has the required enzymatic activity of desaturase, as well as the at least 150 amino acid long fragment of a sequence having at least 50% identity of SEQ ID NO: 2, said fragment having desaturase activity. Thus, the claimed polypeptides are insufficiently described in the

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disclosure. Thus, one skilled in the art cannot reasonably conclude that the Applicants had possession of the claimed invention at the time the instant application was filed.

In addition, claim 2 is directed to a polypeptide of claim 1, wherein said polypeptide has a cytochrome domain. The claim is directed to a large and variable genus of polypeptides comprising any domain of any cytochrome from any organism or man-made, whereas the specification teaches only one representative of the genus, i.e. SEQ ID NO: 2 comprising the domain of cytochrome b₅, said domain having the structure underlined in Fig. 2 b, which is a species of the structure disclosed on page 5, line 13-14. The specification fails to present any identifying characteristics of any domain of any cytochrome other than the described domain of cytochrome 5. Therefore, one skilled in the relevant art is not convinced that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Furthermore, claim 5 is rejected because applicants fail to disclose any desaturase of claim 1 having at least three histidine boxes. Applicants' invention, the desaturase of SEQ ID NO: 2, has only two histidine boxes as marked in Fig. 1.

Also, claims 8, 9, 10 and 11 are rejected because the scope of the claims comprises desaturase of claim 1 which occurs naturally in any organism that does not accumulate gamma-linoleic acid, in any eucaryote, any animal, or any nematode. Thus, claims 8, 9, 10 and 11 are directed to millions of enzymes, whereas Applicants' invention is desaturase of SEQ ID NO: 2 from nematode *C. elegans*. Applicants did not describe desaturases occurring naturally in any organism, except for *C. elegans*,

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that does not accumulate gamma-linoleic acid, in any eucaryote, any animal, or any nematode, thus, the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In their response Applicants write, "The written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics" (page 6, line 3). However, Applicants disclosure does not meet these requirements, because their invention, as claimed by claim 1 and dependent claims, is not complete by disclosure of sufficiently detailed, relevant identifying characteristics. Neither the complete nor partial structure of polypeptides of claim 1 is disclosed in the specification with exception for SEQ ID NO: 2. Also, Applicants fail to set forth correlation between the function and structure for SEQ ID NO: 2. The sequence having the length of at 150 amino acid of SEQ ID NO: 2 or of the sequence having 50% identity to SEQ ID NO: 2, and any fragment of SEQ ID NO: 2, having desaturase activity are not disclosed. In conclusion, one skilled in the art is not convinced that the applicant had possession of the claimed invention at the time the instant application was filed.

2.3.2. *Scope of enablement*

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Claims 1-14 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *C.elegans* Δ^6 desaturase set forth by SEQ ID NO: 2, does not reasonably provide enablement for any polypeptide having desaturase activity, wherein said polypeptide comprises:

- b) a polypeptide having one or more amino acid deletions, insertions or substitutions relative to SEQ ID NO: 2, but having at least 50% amino acid sequence identity therewith;
- c) is a fragment of SEQ ID NO: 2 or polypeptide b) which is at least 150 amino acids long.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are directed to any desaturase comprising SEQ ID NO: 2, its variants having at least 50% identity to SEQ ID NO: 2 and fragments having at least 150 amino acid of sequence described under (b) or SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins and their properties broadly encompassed by the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)), otherwise undue experimentation is necessary.

Factors to be considered in determining whether undue experimentation is required to make the claimed invention are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any desaturase

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from any natural source, or man-made, that comprises a polypeptide having at least 50% identity to SEQ ID NO: 2, or comprises its fragment of at least 150 amino acid of such sequence, or consists of a fragment of SEQ ID NO: 2 and has desaturase activity.

Although the methods of gene cloning and manipulation are well developed and skills of artisans are high, it is not a routine in the art to clone all possible desaturases from all natural or man made sources and select those that are at least 50% identical to SEQ ID NO: 2. Also, it is not a routine experimentation in the art to modify SEQ ID NO: 2 by making deletions, insertions and substitutions resulting in a protein that has 50% identity to SEQ ID NO: 2 and desaturase activity. Neither it is a routine experimentation to find a fragment of at least 150 amino acid long with 50% identity to or unknown fragment of SEQ ID NO: 2 that confers the function of desaturase to any polypeptide that comprises said fragment. Neither is a routine to find an at least 150 amino acid fragment of sequence (b) that has desaturase activity. Probability of success in making the invention is very low.

The specification does not support the broad scope of the claims. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The examiner finds that one skilled in the art would require additional guidance, regarding to which desaturase protein of many known, and from which organism, to choose, as well as what is the function to structure relationship for SEQ ID NO: 2 so that the fragment of SEQ ID NO: 2 having desaturase activity could be used to construct the claimed polypeptide. Thus, one skilled in the art needs further guidance as to the rules for performing substitutions, deletions or insertions without an adverse effect on the protein function. Without such guidance, the experimentation left to those skilled in the art is undue.

In their response, page 10, line 16, Applicants write that the specification provide guidance "as to which specific amino acid substitutions can be performed to arrived at functional desaturases. (Specification at page 7, line 21 through page 8, line 2."

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The quoted passage of the specification refers to the so-called "conservative" or "semi-conservative" substitutions of one amino acid by another. However, Applicants do not teach which particular residues of SEQ ID NO: 2 may be conservatively substituted without the change in function of that protein, because the structure to function relationship is unknown for the disclosed protein. Furthermore, Applicants' claims include polypeptides with multiple substitutions in SEQ ID NO: 2 preparation of which is well outside the realm of routine experimentation.

Applicants provide copies of articles describing truncated forms of such proteins as mannose-6-phosphate receptor, calcium receptors, thrombopoietin receptors, chaperone protein GroEL and even deletion mutants of the p53 gene, with the comments that "One of skills in the art could similarly make deletions in the desaturase polypeptide and test its activity" (page 11, line 16).

This argument is found persuasive in case of claim 13 directed to a part of SEQ ID NO: 2 having desaturase activity. Therefore claim 13 is not rejected. However, the rest of the claims are not so limited and thus their scope is not enabled.

2.4. 35 U.S.C., section 102

The rejection of claim 1 made in the previous Office Action, paper No. 14, is withdrawn because it was improper.

3. Conclusion

Claims 39, 40, 41 and 43 are allowed. Claim 13 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The reasons for allowable subject matter are stated in the previous Office Action, paper No. 14.

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As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.


If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

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Patent Examiner


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600
1600